West Nile virus: New modes of transmission

Division of Vector-Borne Infectious Diseases
Centers for Disease Control and Prevention
Fort Collins, Colorado

Epidemic WNME, United States, 2002

- **Western hemisphere's largest arboviral ME epidemic**
  - **2,741 WNME cases**
  - **1,267 WNF / unspecified**

  } 4008 illnesses*

  - **263 deaths**
    - **39 states & D.C.**
- **Largest WNME epidemic *EVER***
- **Spread to Pacific coast**
- **New clinical syndromes**
  - **Acute flaccid paralysis ("West Nile polio")**
- **Five new transmission modes**

*** As of 2/5/2003**

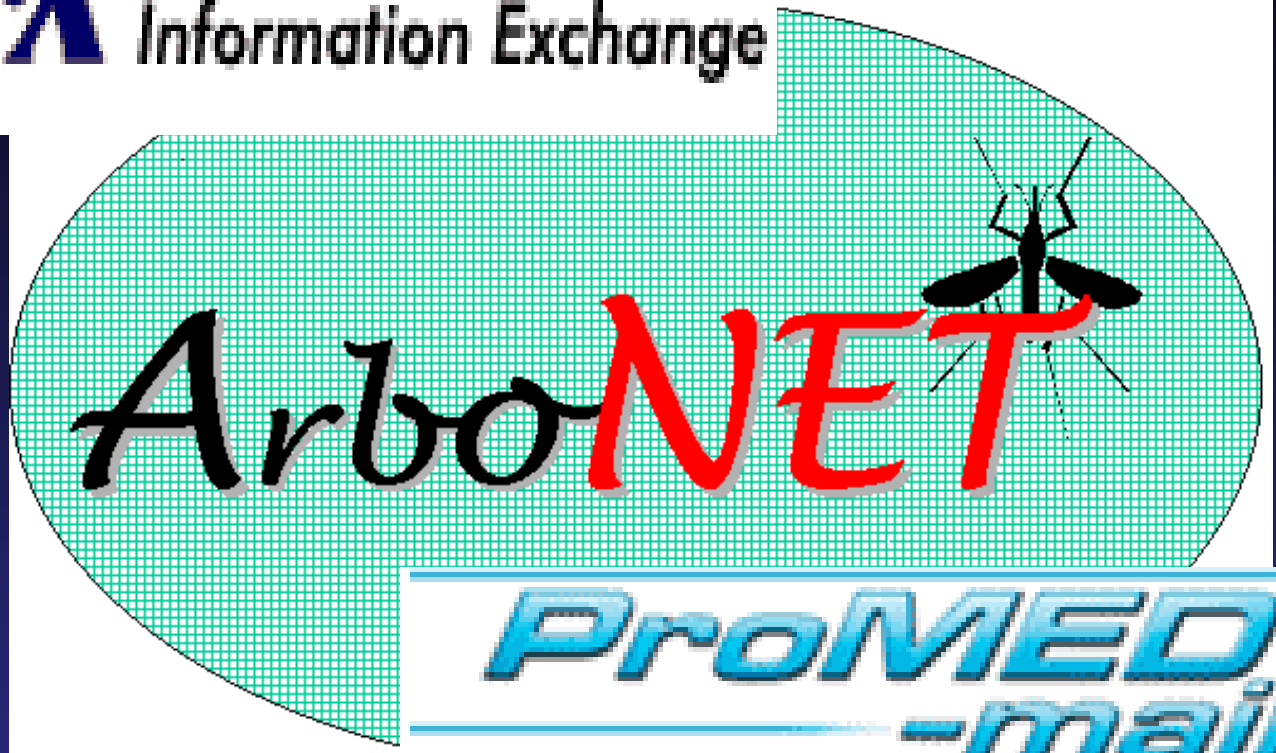
CDC

WN virus infections associated with:

- Transplantation (TPX)
- Transfusion (TFX)
- Breastfeeding
- Transplacental transmission
- Occupational exposure

VECTOR *List-server*

Epi·X The Epidemic Information Exchange



ProMED-mail

Welcome to Epi·X FORUM

CDC

New modes of transmission

- Review previous flavi- and WN virus transmission in animals or humans
- Example of one transmission event
- Summary of reported cases
- Recommendations / comments
- Future surveillance recommendations

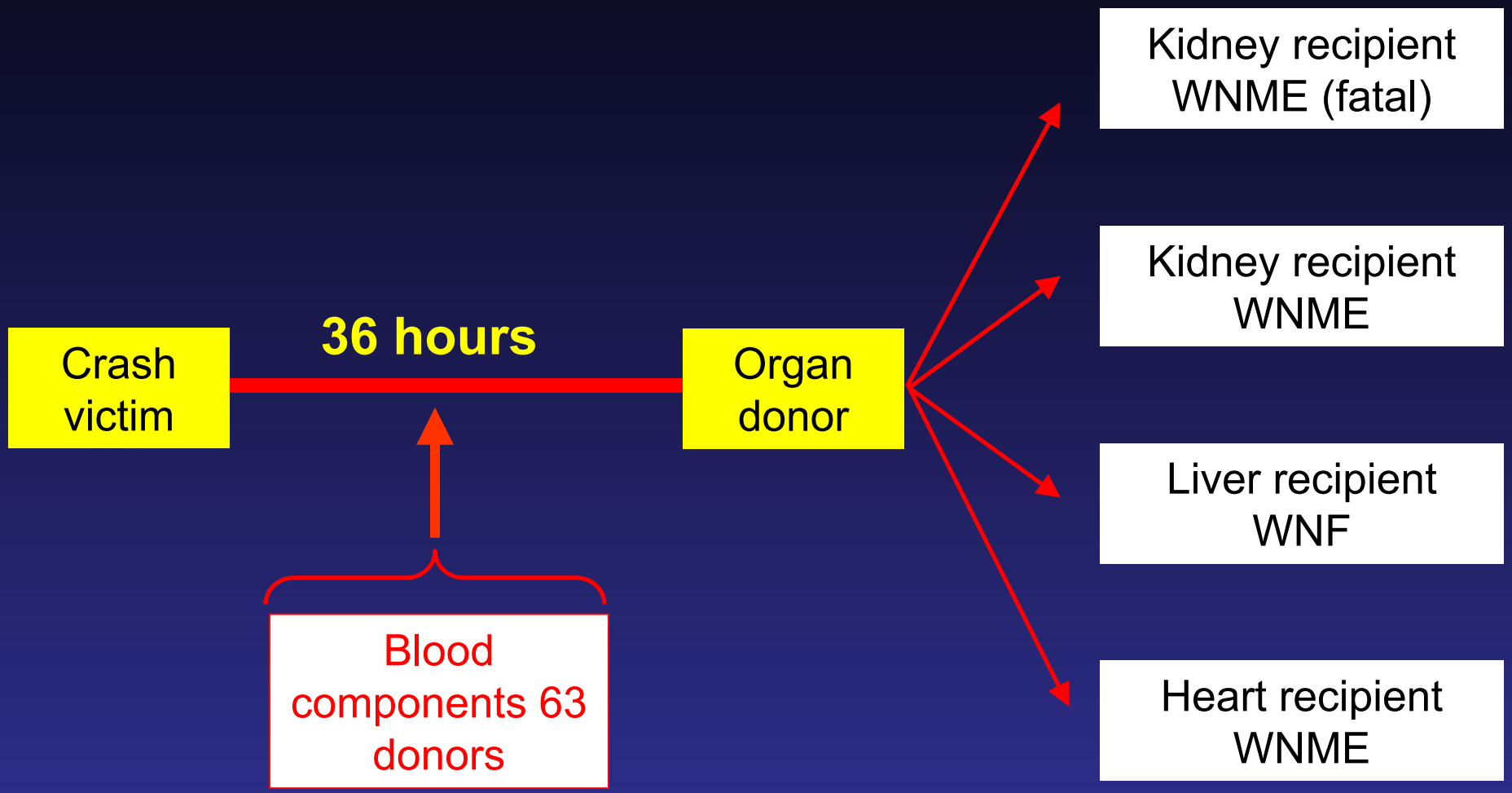
TPX-associated WN virus infection

Previous reports flavivirus transmission

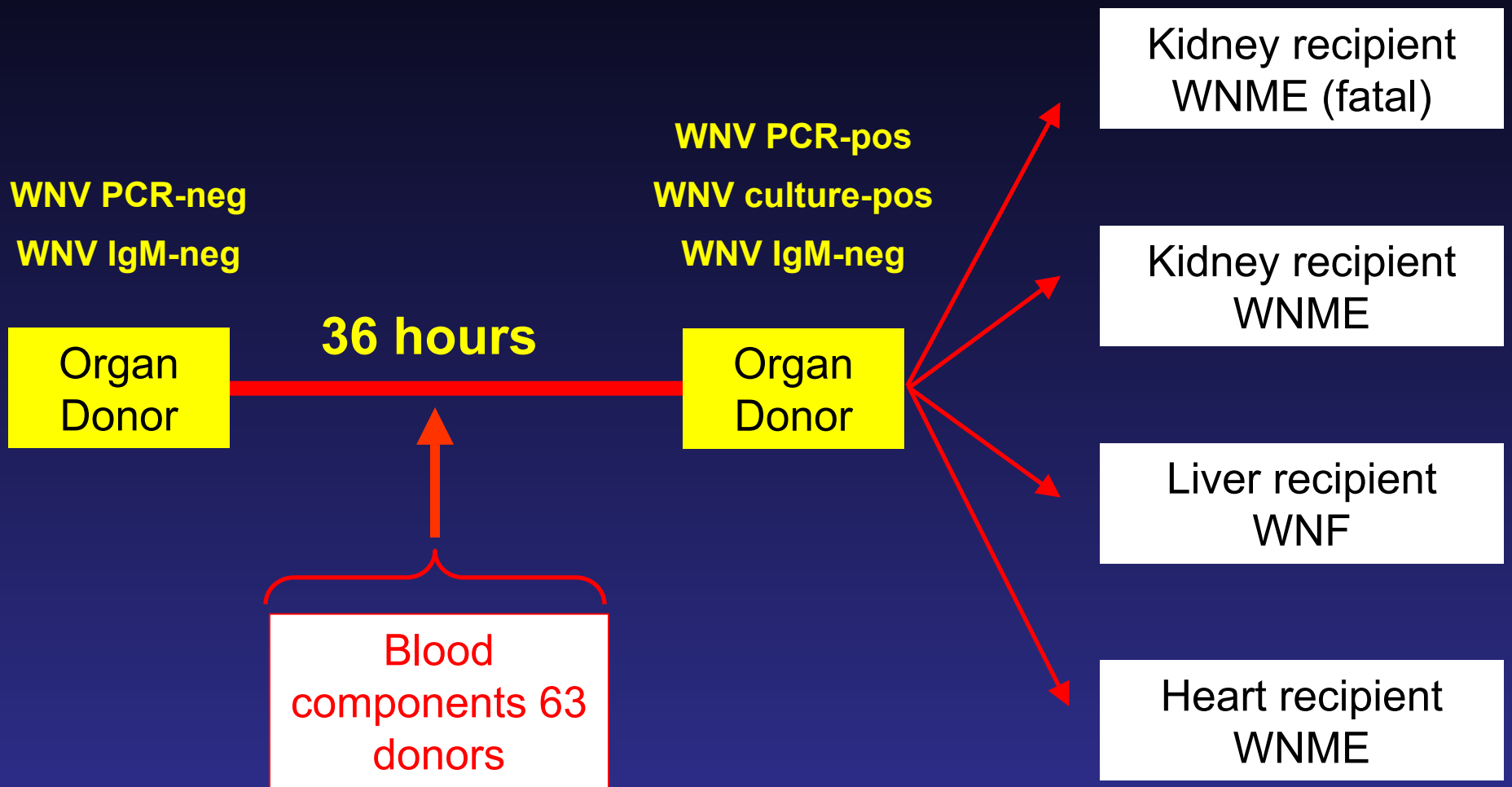
- Except for HCV and HGV, ***NO*** well-documented reports of flavivirus transmission via TPX

- Nov '94: Puerto Rico dengue outbreak – 6 yr old with probable transmission due to bone marrow TPX (Rigau et al AJTMH 2001)

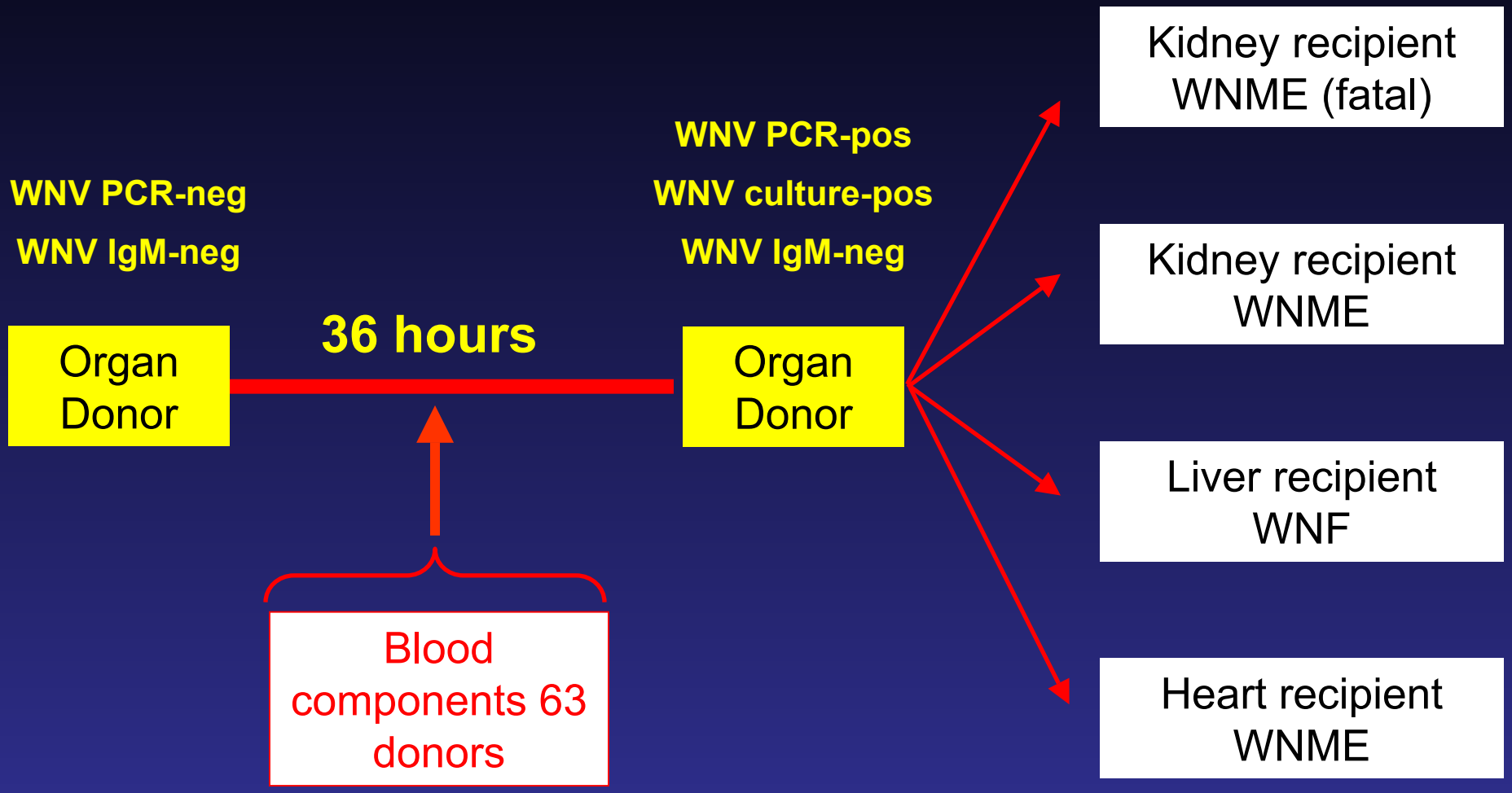
WN virus infection in organ donor and four organ recipients, August 2002



WN virus infection in organ donor and four organ recipients, August 2002



WN virus infection in organ donor and four organ recipients, August 2002



F/U: 1 seroconverting donor;
Retrieved, stored plasma – WNV PCR-positive

CDC

TPX-associated WN virus infection

- TPX-associated transmission confirmed
- High attack rate:
  - 4/4 organ recipients ill
  - 3/4 develop encephalitis
  - Large viral load, immunosuppressive drugs
- Unusual clinical findings:
  - Symptoms 7-17 days post-TPX
  - Minimal CSF pleocytosis observed
- Organ donor's infection from infectious blood unit

CDC

TPX-associated WN virus infection

- Prevention? Exclude viremic organ donors
- Limited exclusion tools:
  - Donor illness? Young infected persons often asymptomatic
  - Serology? Antibodies develop after viremia
  - NAAT blood prior to organ procurement? Virus in kidneys, lungs, spleen, and CNS without viremia
- At a minimum:
  - Report persons who develop WN viral illness within 4 weeks of receiving organ/tissue
  - Assist in retrieval of other potentially infectious tissues

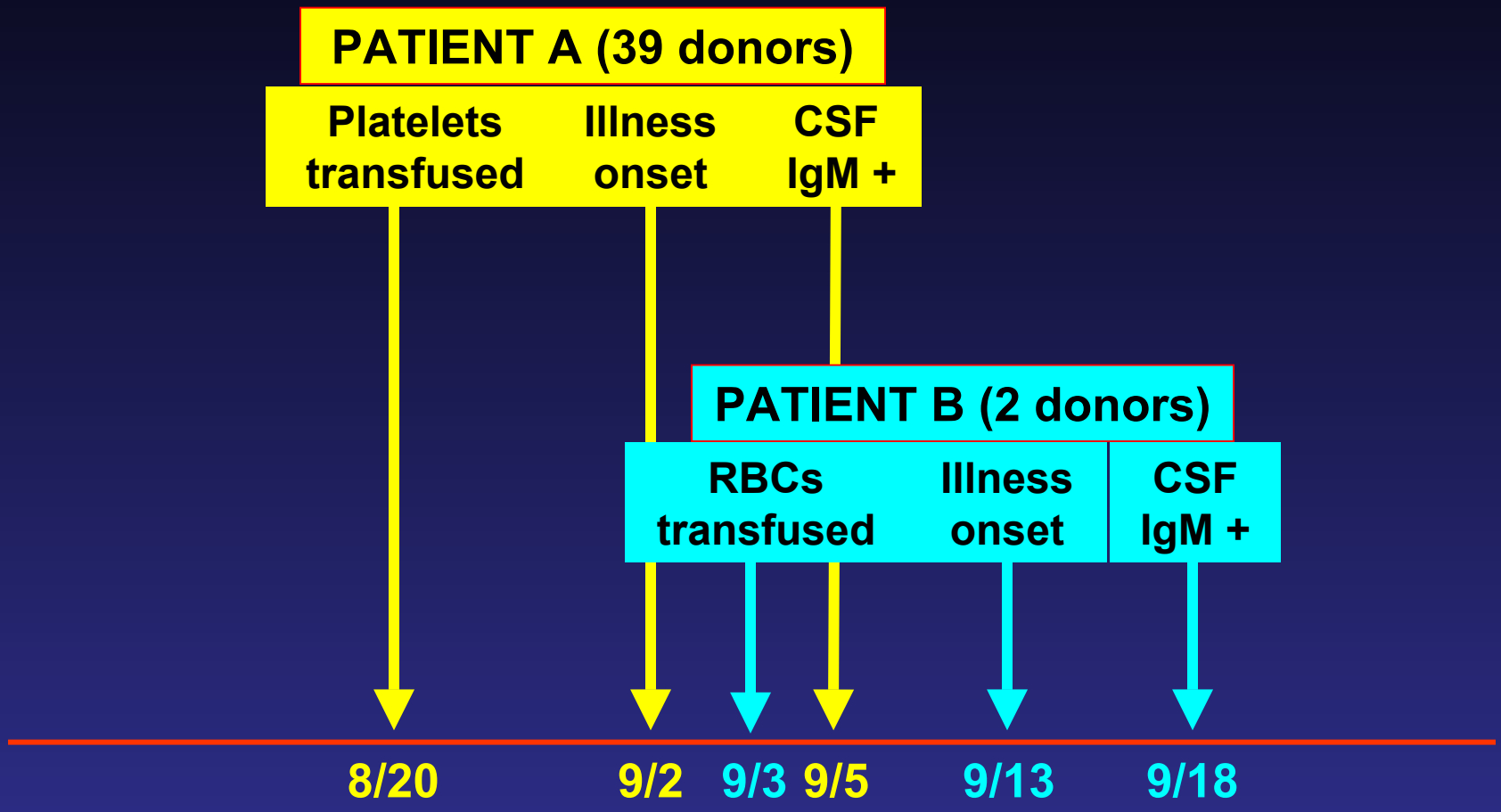
CDC

TFX-associated WN virus infection

Previous reports

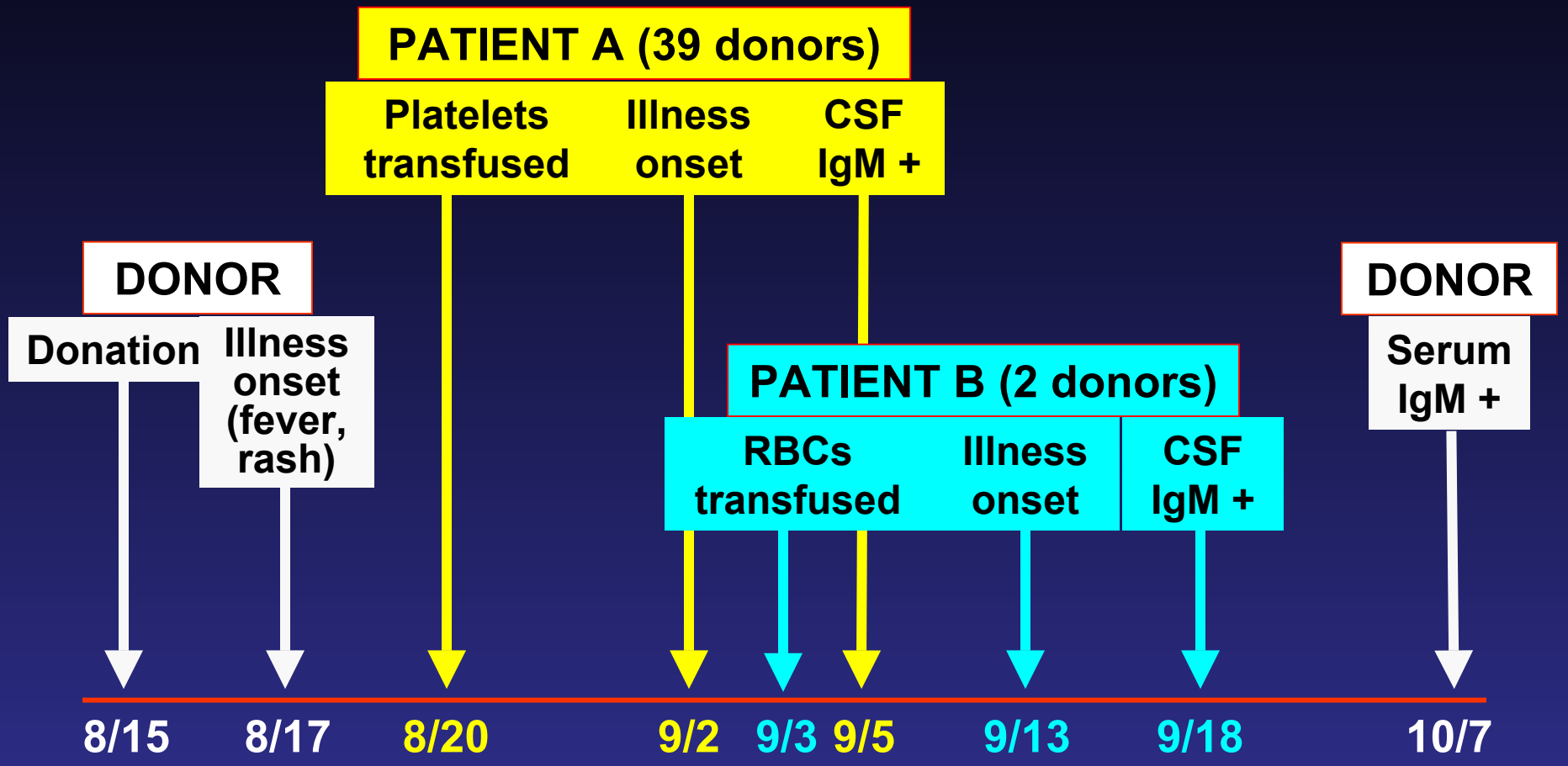
- Except for HCV and HGV, ***NO*** well-documented reports of other flavivirus transmission via TFX

TFX-associated WN viral infection
Patients A (liver transplant) and B (post-partum)



CDC

TFX-associated WN viral infection
Patients A (liver transplant) and B (post-partum)



TFX-associated WN viral infection
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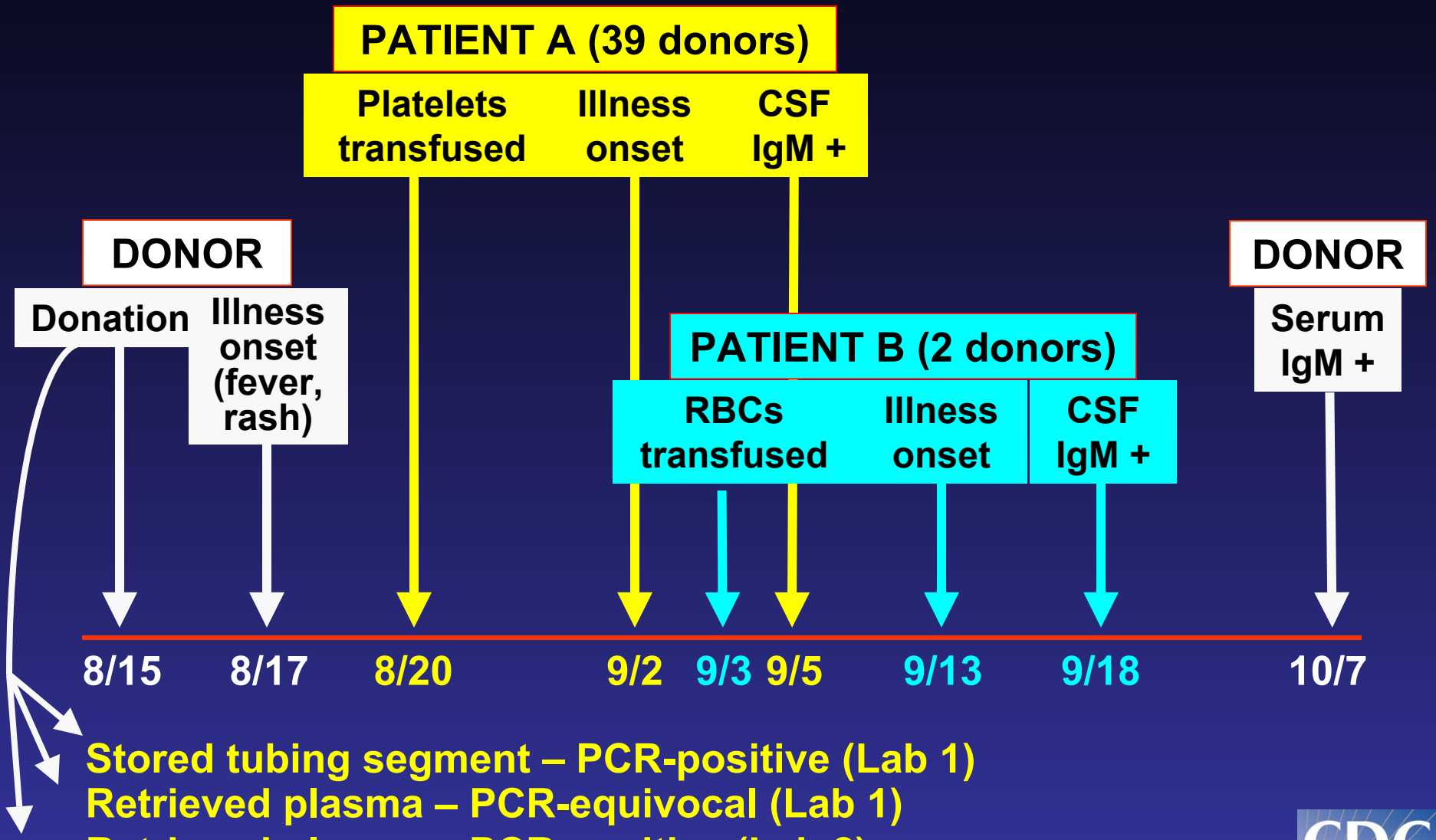


CDC

TFX-associated WN virus infection

- 60 investigations, Aug 2002 - Jan 2003
  - 20 confirmed cases
  - 14 infectious unit donors identified
  - 21 on-going investigations
  - 19 no transmission evidence
  - > 2500 samples tested (NAAT & serology)
- Transmitted in RBCs, plasma, & platelets
- Virus isolated from one stored plasma unit
- 5 of 14 infectious donors **asymptomatic**
- 7 of 20 confirmed cases **asymptomatic**

CDC

TFX-associated WN virus infection

- Reduce risk of TFX-associated transmission
  - Defer unsuitable blood donors
  - Report post-donation illnesses that suggest WN virus infection
  - Withdraw & quarantine blood products from ill donors
- Diagnostics industry developing screening tests
- Testing strategies and deferral policies TBA
- Will need to investigate transfusion cases in 2003 to evaluate strategies and policies

CDC

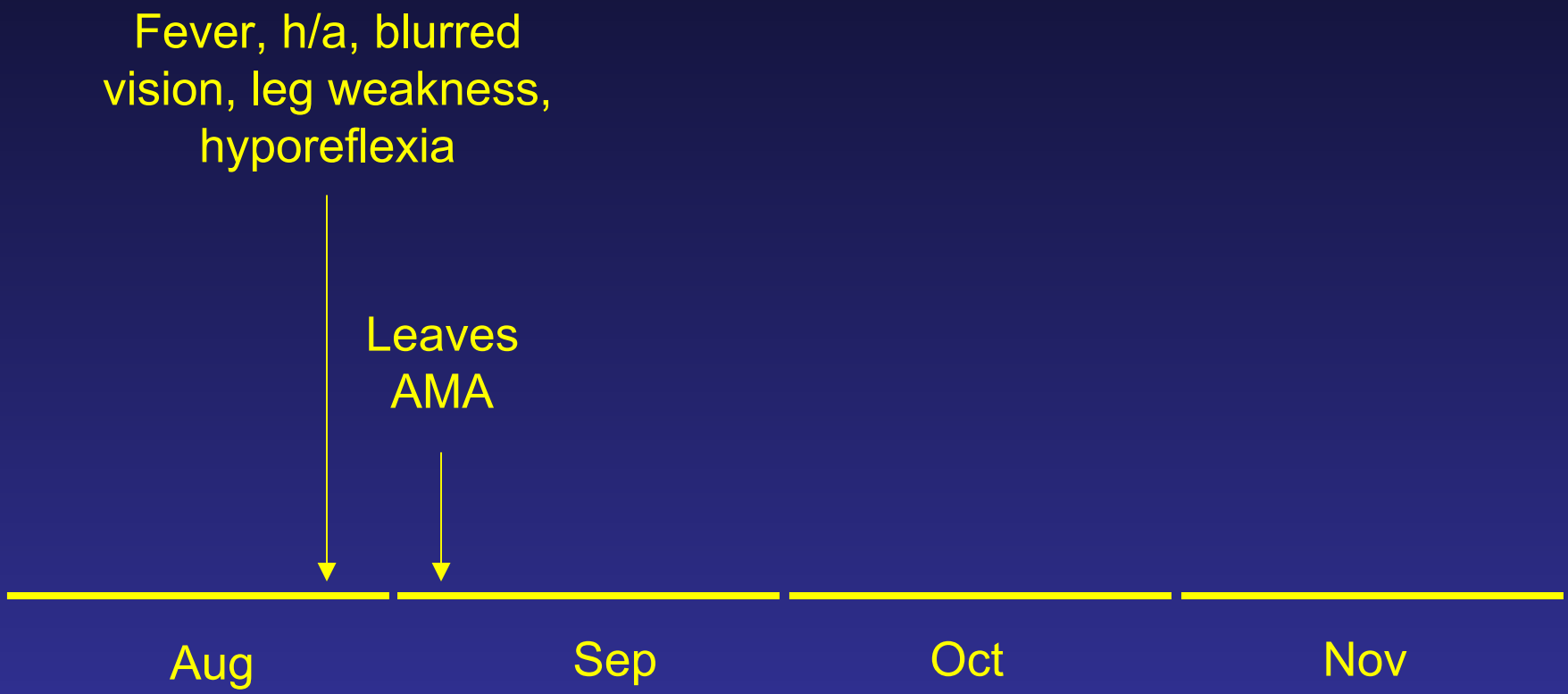
Transplacental WN virus transmission

Transplacental flavivirus transmission

- Human: Vertical dengue transmission
  - Moderate to severe neonatal dengue
- Human: Rare neonatal infections in asymptomatic newborns of YEL vaccinees & YF-infected mothers
- Human: Japanese encephalitis virus
  - Late 70s/early 80s – India
    - 9 cases of infected mothers
    - 4 spontaneous abortions, 4 “normal,” 1 ?
- Previous SLE outbreaks – no neonatal infections reported
- Anecdotal report of WN virus in equine aborted fetuses
- No previous reports of transplacental WN virus infection in humans

CDC

20 year-old pregnant woman



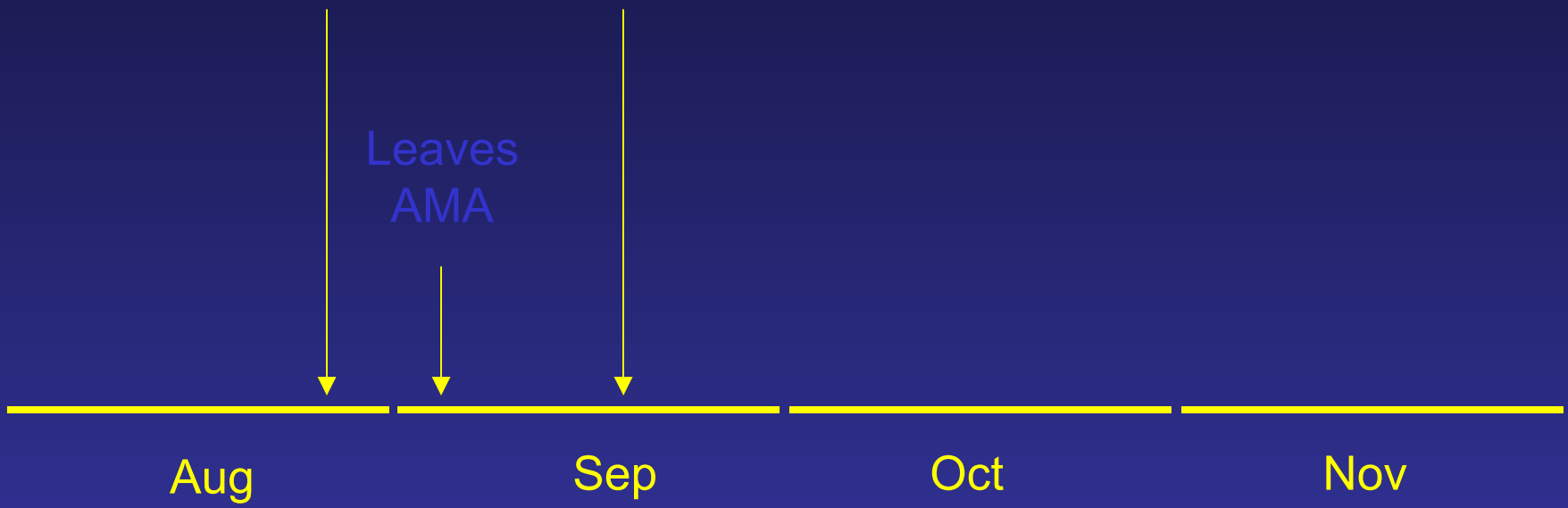
20 year-old pregnant woman

TORCH- & HIV-negative
Flavivirus IgM/IgG (IFA)

Fever (39.3C)
H/A
Blurred vision
Leg weakness
Hyporeflexia

Re-admit;
fall due to
weakness

Leaves
AMA



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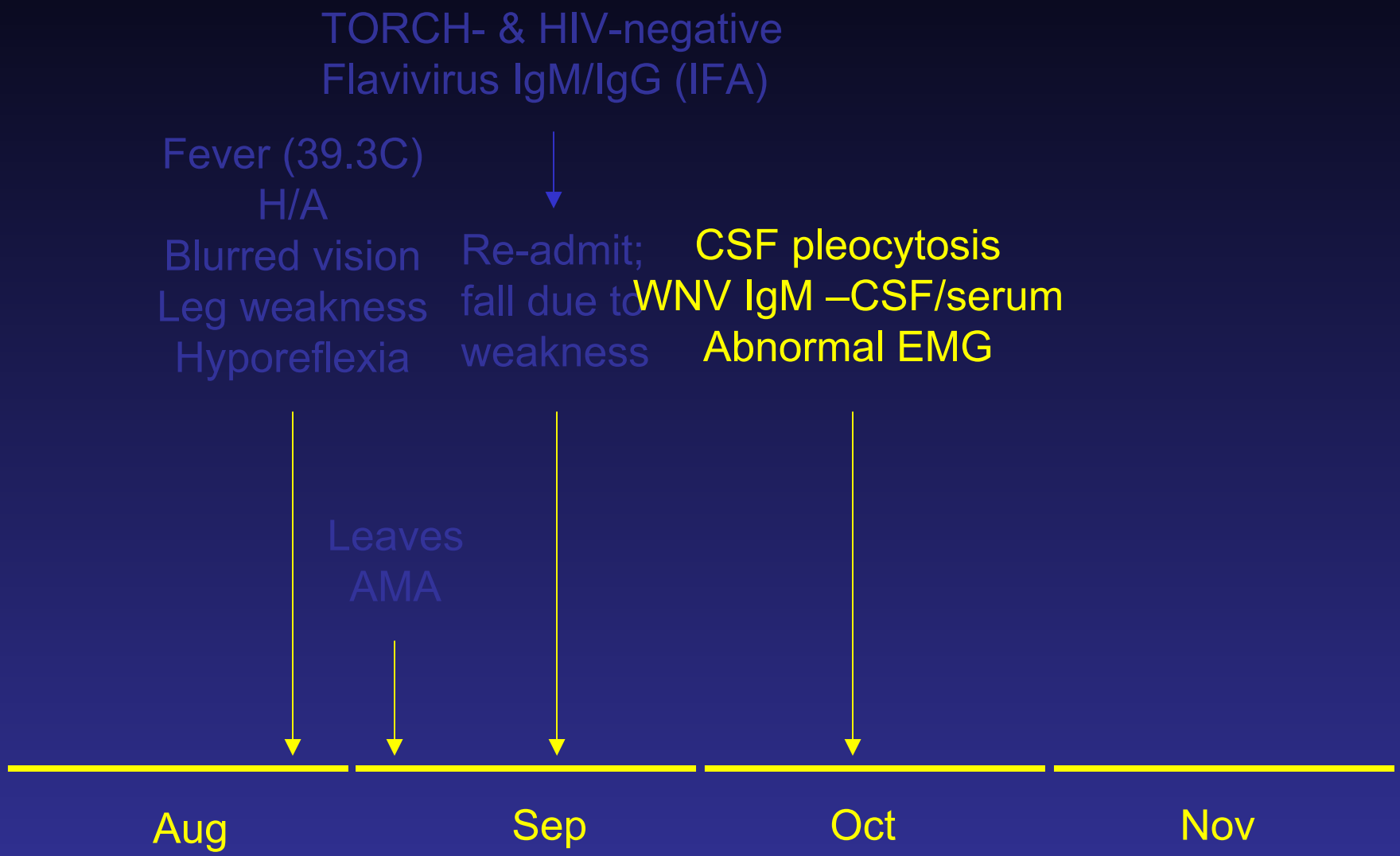
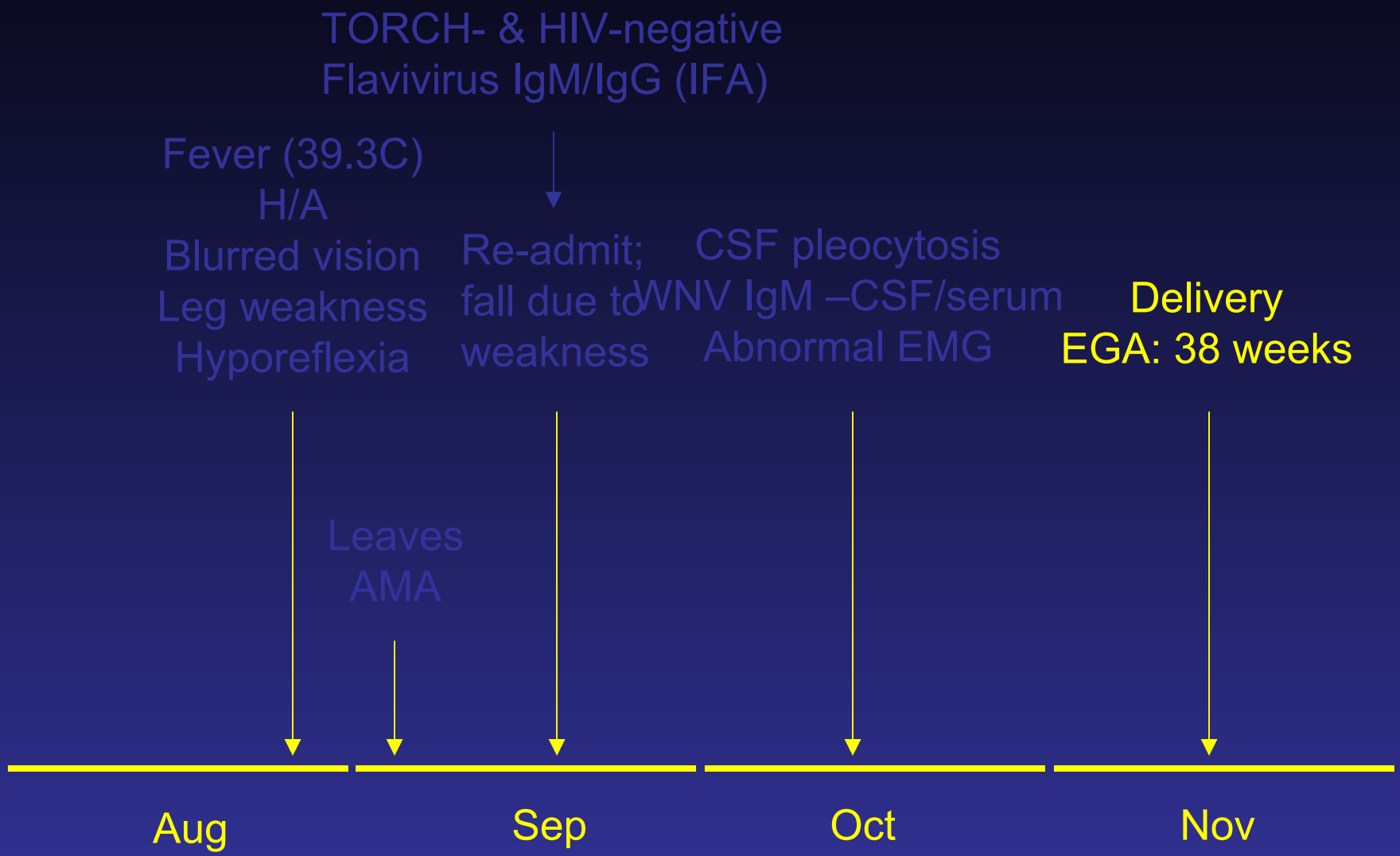


20 year old pregnant woman



Transplacental flavivirus transmission

- Late 2nd trimester infection
- Prolonged clinical illness (viremia?) in mother
- Child:
  - Chorioretinitis; bilateral white matter loss in temporal/occipital; temporal lobe cyst
  - Cord & heel-stick blood – WN virus IgM-positive
  - CSF – WN virus IgM-positive
  - TORCH, CMV, & LCMV antibody negative
  - WN, entero-, & HS viruses all PCR negative
- Placenta/umbilical cord – WN virus PCR positive or equivocal in two labs

CDC

Transplacental flavivirus transmission

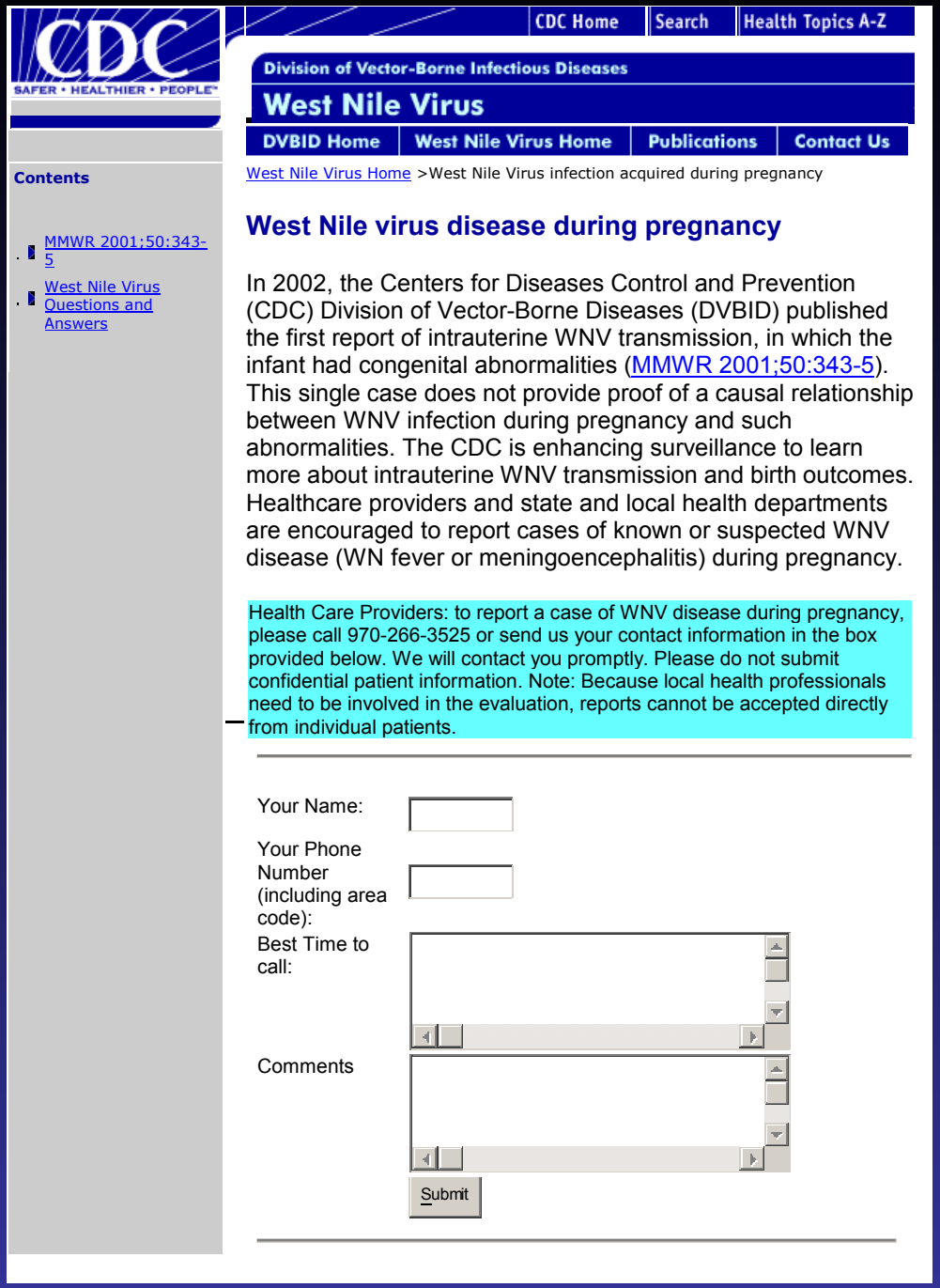
- 1st reported human transplacental transmission of WN virus
- Infection & structural CNS abnormalities – no proven causality
- Recommendations:
  - Infection screening: No
  - Illness testing: Yes
  - Personal protection for pregnant woman: Yes
- Voluntary birth outcome registry

Neonatal outcome among four pregnant woman with WN viral illness

Neonatal illness	Infected	Not infected	Total
Yes	1	0	1
No	0	3	3
Total	1	3	4

Four more pending - 1 unborn; 3 born but illness and infection not yet defined

CDC



Web-based reporting

Health care providers report on-line that they care for a pregnant woman with WN virus infection

States informed when their providers report

Provider contacted; informed of tissues needed for testing

CDC

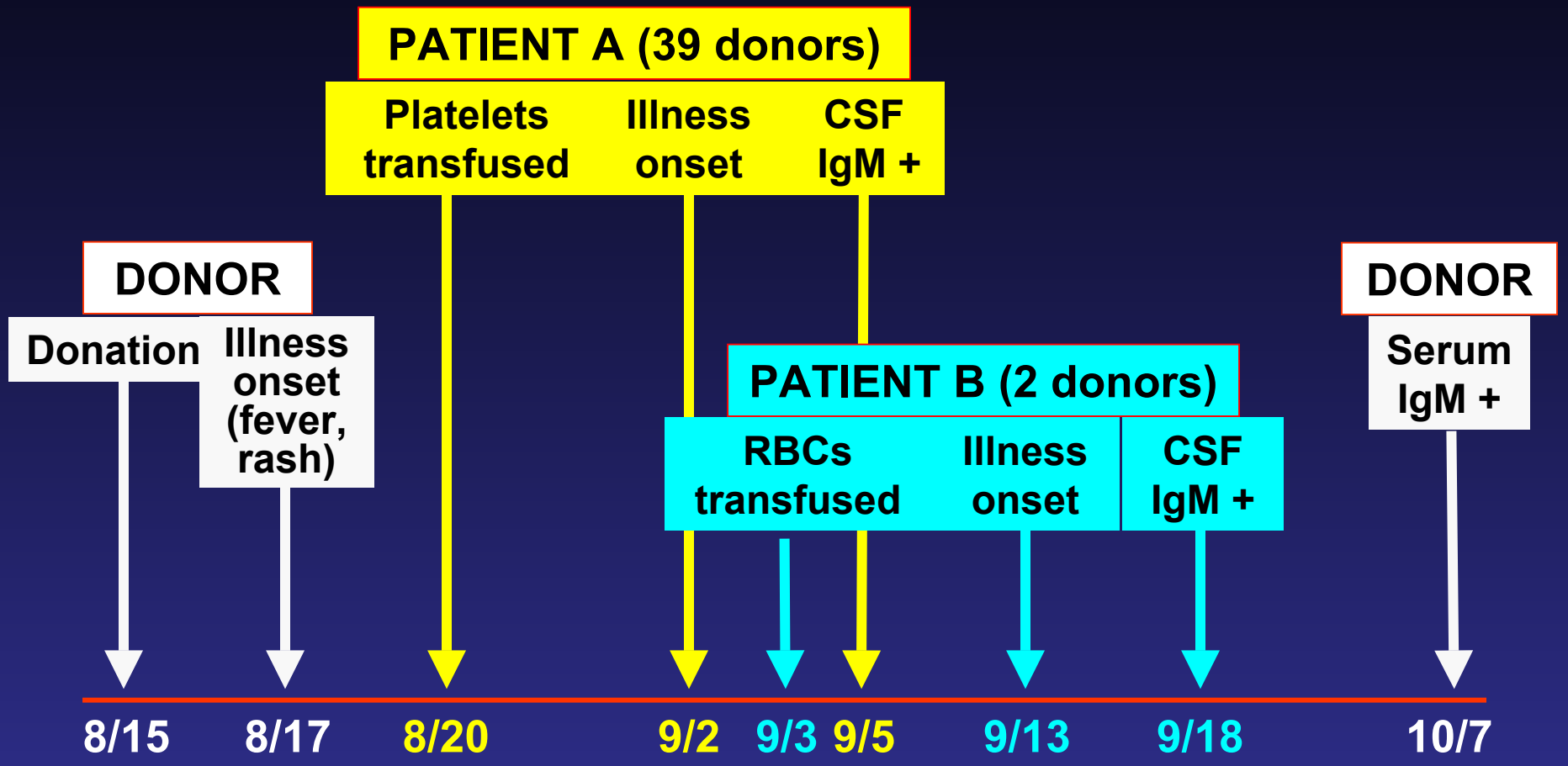
Breastfeeding-associated WN virus infection

Flavivirus transmission in milk

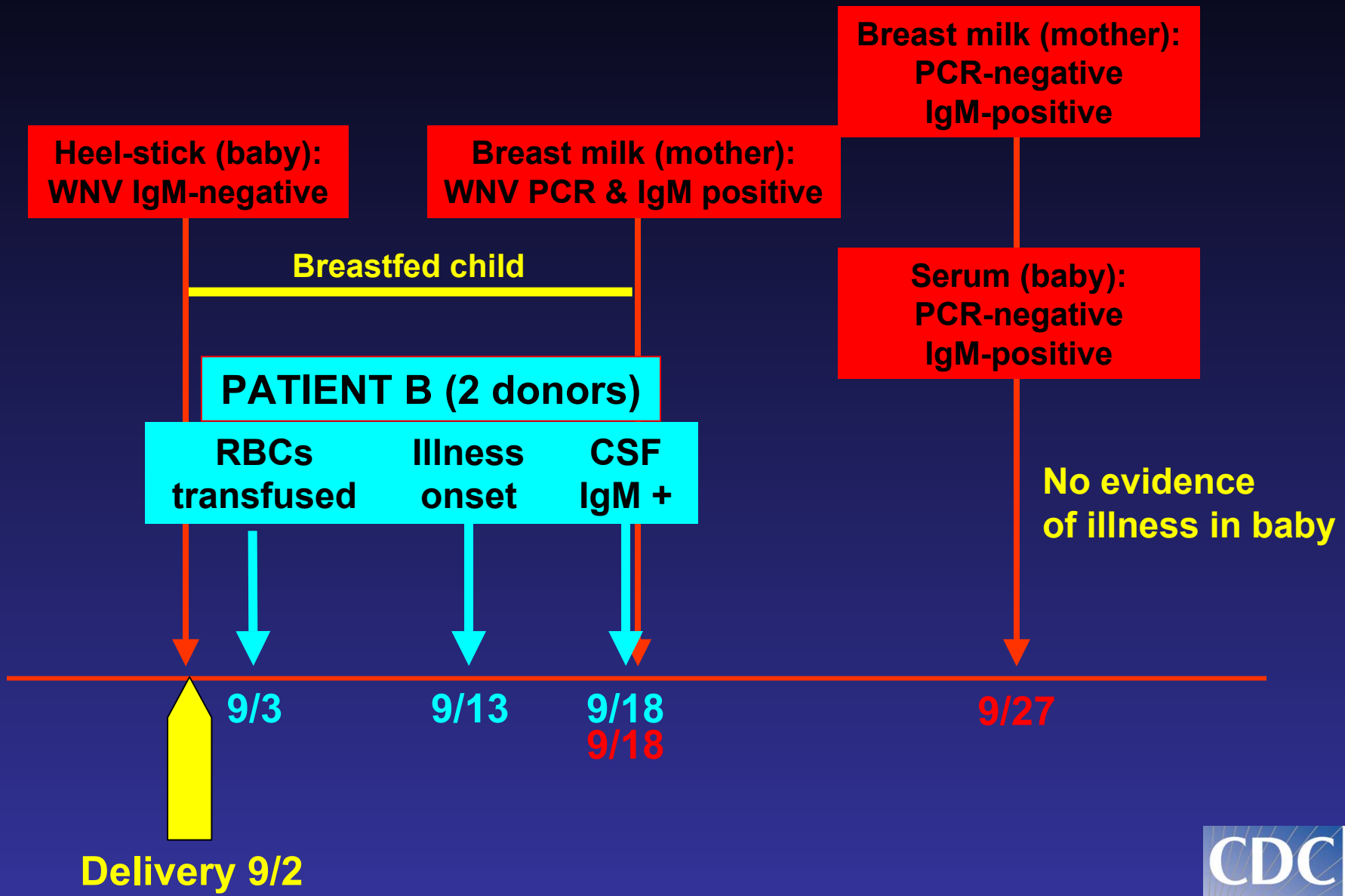
- **Animal-to-animal:**
  - **Powassan virus (experimentally)**
  - **Louping ill virus**
  - **West Nile virus (experimentally; hamsters)**
- **Animal-to-human:**
  - **Tick-borne encephalitis virus (raw sheep & goat milk/cheese)**
- **Primate-to-primate:**
  - **Kyasanur Forest disease virus (langurs)**
- **Human-to-human:**
  - **Hepatitis C virus**

CDC

TFX-associated WN virus infection
Patients A (liver transplant) and B (post-partum)



WN virus transmission in human milk
Patients B (post-partum) and her child



Flavivirus transmission in milk

- 1 of 2 youngest WN virus-infected persons ever; no illness
- No evidence for transplacental infection
  - Mother not infected at delivery
  - WNME 9 days after WN virus-infected unit
- Child breast-fed for first 17 days
- Low titer IgM Ab in human milk
  - Passive transfer of Ab's inefficient
  - WN virus-specific IgM in infant→ independent production
- WN virus genetic material present transiently in milk
  - Attempts to culture WN virus failed

CDC

Flavivirus transmission in milk

- WN viral illnesses in children aged <1 year infrequently reported
- 1999-2001, no reports
- 2002, ***SIX*** persons < 1 year old with WN virus infection reported (excluded one transplacental infection)
- Ages: 0, 1, 3, 6, 9 & 11 mos.
  - 1 asymptomatic (breast feeding-associated)
  - 5 WNME cases
    - 1 breastfed but mother without infection
    - 4 not breast fed in month prior to illness

CDC

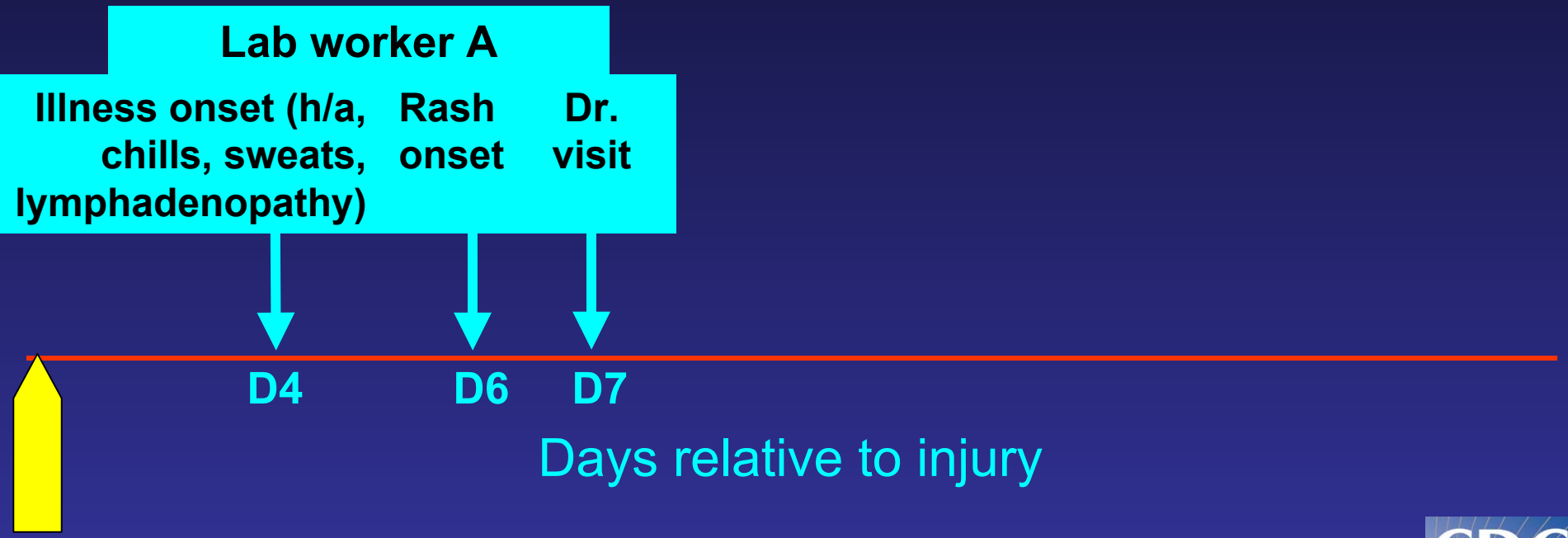
Occupationally-acquired WN virus infection

Occupationally-acquired infection

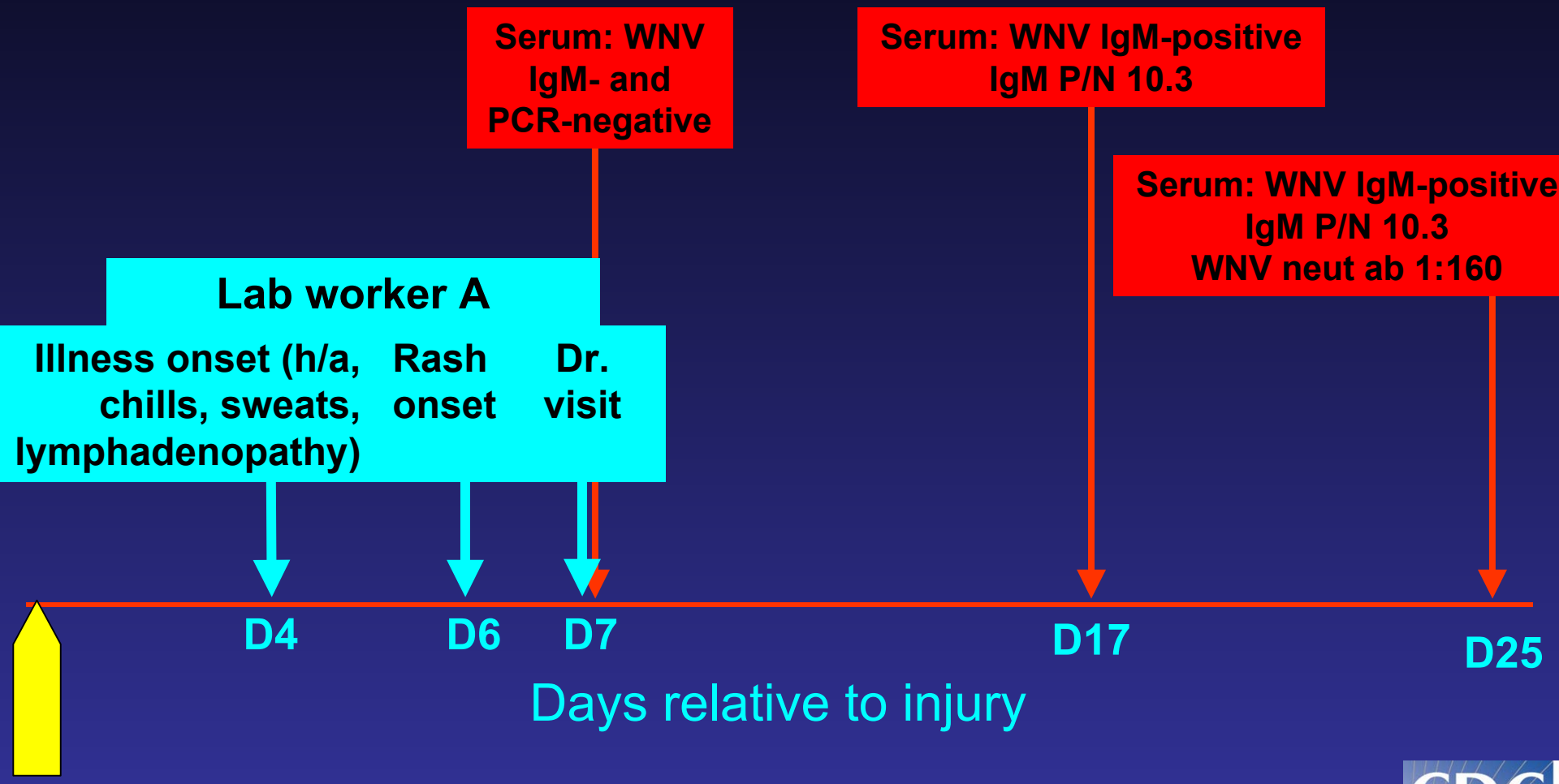
- Occupational transmission of WN and Kunjin viruses among lab workers reported prior to 1999
  - Percutaneous injury
  - Aerosol
- In 2001, suspect case of lab-acquired WN virus infection reported in New York

CDC

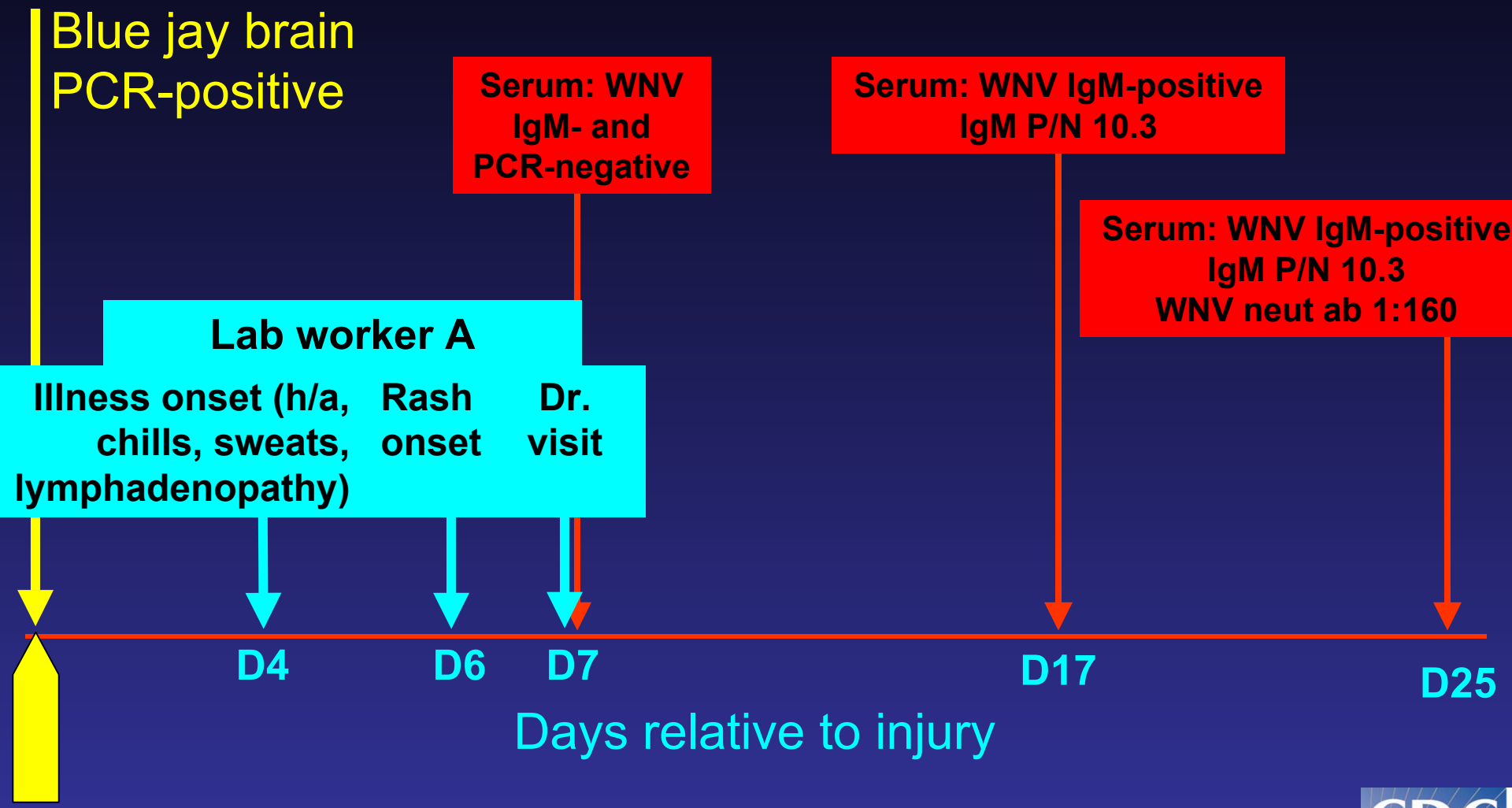
WN viral transmission through percutaneous injury of laboratory worker A



WN viral transmission through percutaneous injury of laboratory worker A



WN viral transmission through percutaneous injury of laboratory worker A



Occupationally-acquired infection

- In 2002, 2 reported cases of occupationally acquired infection among lab workers
- Both percutaneous injury
  - Performing necropsy for WN virus surveillance
  - Making reagents
- Both WN fever
  - Heterologous antibody to closely-related flaviviruses did not protect from illness (ameliorate illness?)

CDC

Occupationally-acquired infection

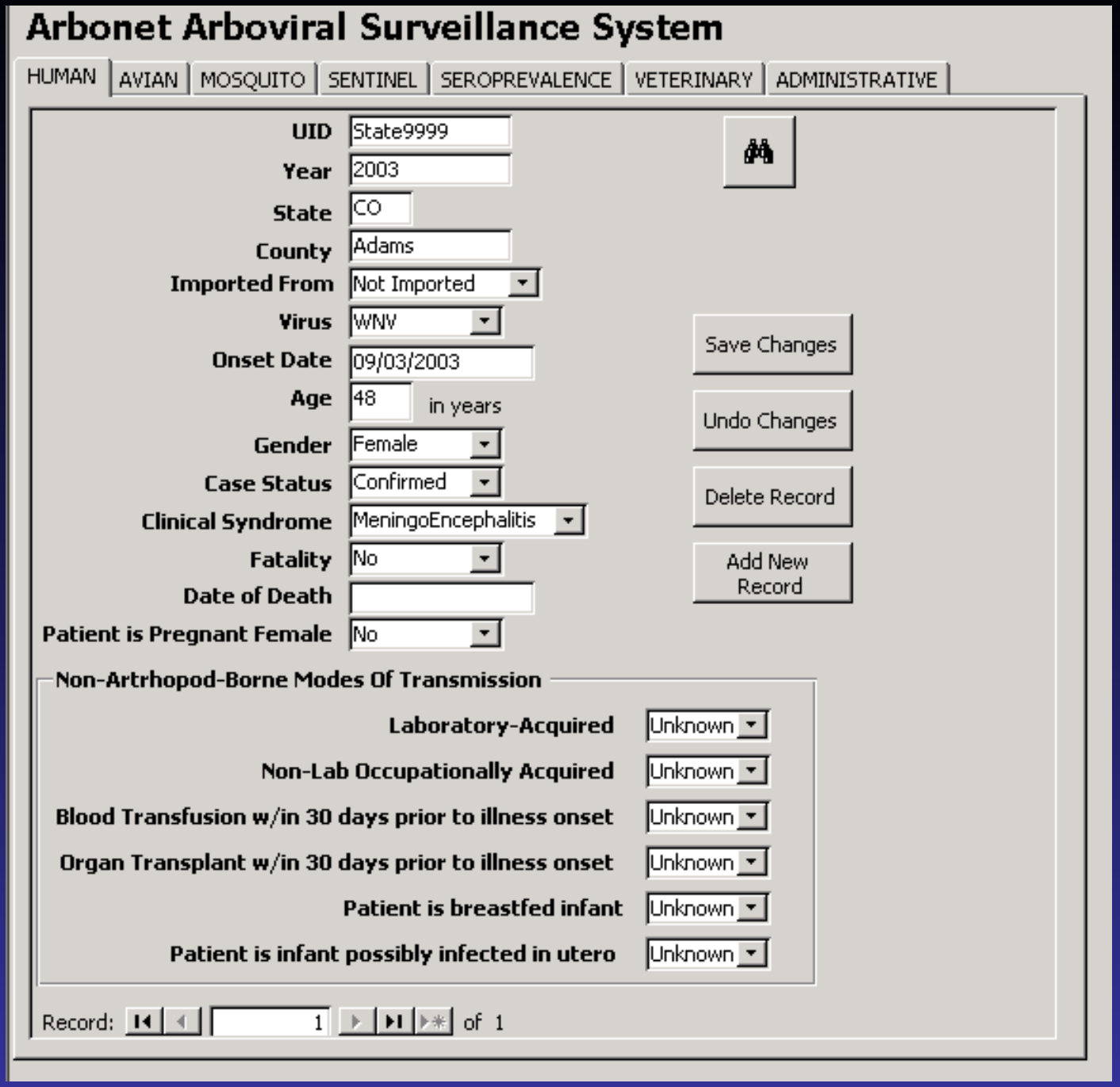
- Anecdotal reports of illness in bird handlers
- Many people working with samples containing live virus
- Goal of surveillance
  - Estimate incidence of work-related infections
  - Define specific activities that result in infection so that protective interventions can be engineered
- Study role of post-exposure treatment

CDC

Surveillance changes

- Abbreviate ArboNET data fields
- Add core data fields, questions to determine if following occurred in specified period before illness:
  - Organ transplantation
  - Blood transfusion
  - Birth
  - Breast feeding
  - Work with known infectious material
- Add field to accommodate these data in local databases
- Add field to accommodate data in ArboNET software and web-based ArboNET
- Rewrite XML file format to accept data transfer from states with other systems

CDC


Arbonet Arboviral Surveillance System
HUMAN
AVIAN
MOSQUITO
SENTINEL
SEROPREVALENCE
VETERINARY
ADMINISTRATIVE
UID
State9999
Year
2003
State
CO
County
Adams
Imported From
Not Imported
Virus
WNV
Onset Date
09/03/2003
Age
48
in years
Gender
Female
Case Status
Confirmed
Clinical Syndrome
MeningoEncephalitis
Fatality
No
Date of Death
Patient is Pregnant Female
No
Save Changes
Undo Changes
Delete Record
Add New Record
Non-Artrhopod-Borne Modes Of Transmission
Laboratory-Acquired
Unknown
Non-Lab Occupationally Acquired
Unknown
Blood Transfusion w/in 30 days prior to illness onset
Unknown
Organ Transplant w/in 30 days prior to illness onset
Unknown
Patient is breastfed infant
Unknown
Patient is infant possibly infected in utero
Unknown
Record:
1
of 1

References

1. Anonymous. Laboratory safety for arboviruses and certain other viruses of vertebrates: the Subcommittee on Arbovirus Laboratory Safety of the American Committee on Arthropod-Borne Viruses. Am J Trop Med Hyg 1980;291:359--81.
2. Pike RM. Laboratory-associated infections: summary and analysis of 3,921 cases. Health Lab Sci 1976;13:105--14.
3. Sewell DL. Laboratory-associated infections and biosafety. Clin Microbiol Rev 1995;8:389--405.

CDC